

AMENDMENTS TO THE SPECIFICATION

Please amend the following paragraphs accordingly

3 - 31

Page 3, lines 8 and 16,

PF 10/3/06

an aromatic group optionally having one or more substituents, the aromatic ring having optional nitrogen, sulfur or oxygen, wherein the substituent is; hydroxy; halogen; alkyloxy; alkyl; amino; alkylamino; carboxyl; nitro; sulfonylamido, alkanesulfonyl; amido; or linear or cyclic C₁-C₆ alkyl optionally having one or more substituents, the alkyl having an optional nitrogen, sulfur or oxygen linkage and the substituentsubstituent of the alkyl being: hydroxy; halogen; alkyloxy; alkyl; amino; alkylamino; carboxyl; nitro; sulfonylamido, alkanesulfonyl; amido; an aromatic group optionally having one or more substituents selected from the group consisting of hydroxy; halogen; alkyloxy; alkyl; amino; alkylamino; carboxyl; nitro; amido; dioxoisooindole; and a sulfonylamino having an aromatic group substituted with hydroxy, halogen, alkyloxy, alkyl, amino, alkylamino, carboxyl, nitro, sulfonylamido, alkanesulfonyl or amido; an aromatic group optionally having one or more substituents selected formfrom the group consisting of hydroxy, halogen, alkyloxy, alkyl, amino, alkylamino, carboxyl, nitro, sulfonylamide, alkanesulfonyl and amido, the aromatic ring containing nitrogen, sulfur or oxygen; or a cyclic C₃-C₈ alkyl optionally having one or more substituents selected from the group consisting of hydroxy, halogen, alkyloxy, alkyl, amino, alkylamino, carboxyl, nitro and amido; or

29-37

Page 3, lines 31 and 37

PF 10/3/06

Among the compounds of formula (I) of the present invention, the preferred are:

those wherein n, R¹, R² and R³ have the same meaningmeanings as defined previously;

R⁴ and R⁵ are each independently hydrogen;

C₁-C₄ alkyl optionally having one or more substituents selected from the group consisting of OH, NH₂, NO₂, and an aromatic group, the aromatic group optionally having one or more substituents selected from the group consisting of OH, C₁-C₄ alkyloxy, NH₂, NO₂, methanesulfonylamino, ethanesulfonylamino, ~~toluenesulfonylamino~~ toluenesulfonylamino and dioxoisoindole; cyclic C₃-

Page 4, lines 3-7, 16, 25, 29, and 32

Bf
10/3/06

C₈ alkyl optionally having one or more substituents selected from the group consisting of OH, NH₂ and NO₂; C₁-C₄ alkyl carrying a morpholine or ~~exopyrrolidine~~ oxopyrrolidine group which is optionally substituted with OH, NH₂, NO₂ or -O-; C₁-C₄ alkyl or C₁-C₄ aminoalkyl carrying a ~~pyrrolpyrrole~~, pyrazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, isoxazole, oxazole, ~~isotiazole~~ isothiazole, ~~tiazolidine~~ thiazoldine, tiazole, 1,2,5-oxadiazole, 1,2,3-oxadiazole, 1,2,5-thiodiazole thiadiazole, 1,2,3-thiodiazole thiadiazole, 1,3,4-oxadiazole, 1,3,4-thiodiazole thiadiazole, pyridine, pyrimidine or triazine group which is optionally having one or more substituents selected from the group consisting of Cl, OH, NH₂, NO₂, C₁-C₄ and phenyl;

cyclic C₃-C₈ alkyl optionally having one or more substituents selected from the group consisting of OH, NH₂ and NO₂;

an aromatic group optionally having one or more substituents selected from the group consisting of OH; NH₂; hydroxyalkyl; aminoalkyl; NO₂; and a C₁-C₄ alkyl group optionally having one or more substituents selected from the group consisting of OH, NH₂, NO₂,

methanesulfonylamino, ethanesulfonylamino, ~~toluenesulfonylamino~~ toluenesulfonylamino,
dioxoisoindole and thiophensulfonylamino; or

form, together with the $-N-(CH_2)_n-$ moiety to which they are attached, a nitrogen heterocycle optionally having one or more substituents selected from the group consisting of OH, NH₂ and NO₂, the heterocycle containing 1 to 3 nitrogen, sulfur or oxygen atom.

In the present invention, the compounds of formula (I) as the below are most preferred: those wherein n, R¹, R² and R³ have the same meaning meanings as defined previously; R⁴ and R⁵ are each independently hydrogen;

C₁-C₄ alkyl optionally having one or more substituents selected from the group consisting of OH, NH₂, NO₂, morpholine, nitropyridineamino, pyridine, ~~exopyrrolidinoxopyrrolidine~~, imidazole optionally having a Cl, CH₃ or phenyl substituent; and phenyl optionally having one or more substituents selected from the group consisting of OH, NH₂, methoxy, NO₂, methanesulfonylamino, ethanesulfonylamino, ~~toluenesulfonylamino~~ toluenesulfonylamino and dioxoisoindole;

Page 5, line 8

NH₂, NO₂, methanesulfonylamino, ethanesulfonylamino,
~~toluenesulfonylamino~~ toluenesulfonylamino, dioxoisoindole or thiophensulfonylamino
substituent; or

Page 15, lines 4-5

wherein, p-TSA is *p*-toluenesulfonic acid, DMF is dimethylformamide, THF is tetrahydrofuran, TFA is trifluoroacetic acid, EDCI is ethyl-dimethylaminopropyl-carbodiimide

hydrochloride, DMAP is 4-dimethylaminopyrdine, HOBr is N-

hydroxybezotriazole hydroxybenzotriazole, n, R¹, R², R³, R⁴ and R⁵ have the same meaning meanings as defined previously.

18-37
Page 16 , lines 21 and 36

b7f
10/3/06

As shown in Scheme II, the compound of formula (Ib) can be prepared by reacting 3-amino-4-methoxy benzoic acid (compound II) and an alcohol (e.g., methanol or ethanol) to obtain compound (III), adding p-toluenesulfonic acid, benzene and 4-nitrobezonitrile nitrobenzonitrile thereto, refluxing the mixture at 80 to 200 °C, adding NaOCl thereto at room temperature and purifying by silica gel column chromatography to obtain compound (XI); dissolving the compound (XI) thus obtained in an organic solvent, adding an aqueous alkali solution (e.g., Na₂CO₃ solution) thereto, refluxing the mixture and purifying by silica gel column chromatography to obtain compound (XII); dissolving the compound (XII) thus obtained in an alcohol, adding Pd/C thereto and refluxing the mixture to obtain compound (XIII); dissolving the compound (XIII) thus obtained in an organic solvent, adding a base (e.g., CsCO₃, Na₂CO₃, NaHCO₃, K₂CO₃ or KHCO₃), 2-chloroethylmorphine and potassium iodide thereto and stirring the mixture at room temperature to obtain compound (XIV); dissolving the compound (XIV) obtained thus in an organic solvent, adding an alkali hydrate, stirring the mixture at room temperature to obtain compound (XV); dissolving the compound (XV) thus obtained in an organic solvent, adding ~~4,5-dichloro-1-(3-aminopropyl)imidazole-4,5-dichloro-1-(3-aminopropyl)imidazole~~ and a coupling agent (e.g., EDCI, DMAP or HOBr), stirring the mixture at room temperature and purifying by silica gel

Page 19, line 15

PF
10/3/06

Anhydrous *p*-toluene sulfonic acid (41.99 g, 220.8 mmol) was melted at 120 °C and 3-amino-4-methoxy benzoic acid methyl ester (20 g, 110.38 mmol) obtained in step 1 and benzonitrile (22.77 g, 220.8 mmol) were added thereto and stirred at 180 °C for 5 hours. The resulting solution was cooled to room temperature and the reaction was stopped by adding NaHCO₃ thereto. The resulting mixture was extracted with ethyl acetate, the extract was dried over MgSO₄ and concentrated under a reduced pressure. The concentrate was dissolved in 50% methanol and 5% NaOCl (56 mL, 37.65 mmol) was added dropwise thereto. After 5 min, the resulting mixture was extracted with ethyl acetate, the extract was dried over MgSO₄ and concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography (eluent – MeOH/CDCl₃ = 5 : 95, Merck, Silicagel 60) to obtain the title compound (31 g, 25.10 mmol) in a yield of 88%.

Page 21, line 37

PF
10/3/06

Anhydrous *p*-toluene sulfonic acid (41.99 g, 220.76 mmol) was melted at 120 °C and 3-amino-4-methoxy benzoic acid methyl ester (20 g, 110.38 mmol) obtained in step 1 of Preparation Example 1 and 4-chlorobenzonitrile (22.78 g, 165.57 mol) were added thereto and stirred at 160 °C for 8 hours. The resulting solution was cooled to room temperature and the reaction was stopped by adding 1M NaHCO₃ thereto. The resulting mixture was extracted with ethyl acetate, the extract was dried over MgSO₄ and concentrated under a reduced pressure. The concentrate was dissolved in 500 ml of 50% methanol and 5% NaOCl (197 mL, 132.46 mmol) was added dropwise thereto. After 5 min, the resulting mixture was extracted with ethyl acetate,